What is the relationship between glycemic index or glycemic load and cardiovascular disease?

Conclusion

Due to limited evidence, no conclusion can be drawn to assess the relationship between either glycemic index or load and cardiovascular disease.

Grade: Limited

Overall strength of the available supporting evidence: Strong; Moderate; Limited; Expert Opinion Only; Grade not assignable For additional information regarding how to interpret grades, click here.

Evidence Summary Overview

Although the evidence for an association between high glycemic index or high glycemic load and cardiovascular disease (CVD) is more negative than positive, the evidence available is inadequate to come to a firm conclusion on this question.

Eight reports have been published since 2000 (Beulens, 2007; Kaushik, 2009; Levitan, 2007; Liu, 2000; Halton, 2006; Oh, 2005; Tavani, 2003; van Dam, 2000). Of these, three are from the same Nurses' Health Study. After 10 years of follow-up, Liu et al (2000) reported glycemic index was associated with CVD. A high glycemic load was associated with CVD in women with a body mass index (BMI) greater than 23, but not with a BMI less than 23kg/m^2. After 20 years of follow-up, Halton (2006) reported both a high glycemic index and load to be associated with CVD. Oh (2005) reported on the associations between dietary carbohydrate, glycemic index, glycemic load and stroke. They found no association between glycemic index and stroke. They found a positive association between glycemic load and total stroke in women with a BMI greater than 25, but not in those with a BMI less than 25kg/m^2.

Five other reports are available. Of these, Beulens (2007) found a positive trend for an association between glycemic load and stroke, but not for glycemic index and stroke. He found a positive trend between glycemic index and CHD and between glycemic load and coronary heart disease (CHD) only for women with a BMI greater than 25kg/m^2.

Kauschik (2009) found an association between both glycemic index and glycemic load and death from stroke. Levitan (2007) found no association between glycemic index or glycemic load with myocardial infarction (MI), ischemic stroke or all-cause mortality. van Dam (2000) found no association of either glycemic index or glycemic load and CHD.

One case-control study (Tavani, 2003) reported on the relation between glycemic index and glycemic load and the risk of non-fatal acute MI. No significant (NS) association was found.

Evidence Summary Paragraphs

Beulens, 2007 (positive quality), a cohort study in the Netherlands, prospectively assessed whether high dietary glycemic load (GL) and glycemic index (GI) were associated with an increased risk of

CVD in 15,714 Dutch women who were 49 to 70 years, without diabetes or CVD and were participants of the Prospect-EPIC cohort study. Subjects were followed for 9±2 years (141,633 person-years). A total of 556 cases of CHD and 243 cases of cerebrovascular accident occurred. After adjustment for CVD risk factors and dietary variables, both GL with a hazard ratio (HR) of 1.47 (95% CI: 1.04, 2.09; P=0.03), and GI with HR of 1.33 (95% CI: 1.07, 1.67; P for trend = 0.02) were associated with increased risk of cerebrovascular accident. In women with BMI higher than 25kg/m^2, GL was associated with CVD (HR=1.78, 95% CI: 1.11, 2.85; P=0.04) but not with normal weight women. Glycemic index was associated with CHD (P=0.01) and not cerebrovascular accident; in addition, BMI did not modify the association of GI with CVD.

Kaushik, 2009 (positive quality), cohort study in Australia, prospectively investigated the links between diets with high glycemic index (GI), low cereal fiber (CF) and the greater risk of stroke-related mortality and retinal microvascular caliber in 2,712 Australians 49+ years and participants of the Blue Mountains Eye Study. Dietary GI was assessed at baseline using a validated food-frequency questionnaire (FFQ) and followed for 13 years. Ninety-five (3.5%) participants died from stroke. After adjusting for multiple stroke risk factors, increasing GI (HR=1.91; 95% CI: 1.01, 3.47) and decreasing CF (HR=2.13; 95% CI: 1.19, 3.80) predicted greater risk of stroke death, while there was no relationship between total fruit or vegetable fiber and risk of stroke-related death. Participants consuming food in the highest GI tertiles and lowest CF tertiles had a five-fold increased risk of stroke death (HR=5.06, 95% CI: 1.67, 15.22). High-GI and low-CF diets predict greater stroke mortality and wider retinal venular caliber.

Levitan, 2007 (positive quality), a cohort study in Sweden, prospectively examined the association between dietary glycemic index (GI) and glycemic load (GL) with CVD among 36,246 Swedish men who were 45 to 79 years old and free of diabetes or prior CVD. Dietary GI and GL were assessed at baseline and followed for six years. Dietary GI and dietary GL were not associated with MI (N=1,324), ischemic stroke (N=692), cardiovascular mortality (N=785) or all-cause mortality (N=2,959). However, dietary GL was associated with hemorrhagic stroke [N=165; RR=1.44 comparing extreme quartiles (95% CI: 0.91, 2.27; P=0.047)]. No association between dietary GL with all-cause mortality was observed. Among men with cereal fiber (CF) intake of 12.8g per day or men with lower CF intake, higher dietary GL was associated with an elevated risk (trends not statistically significant). Overall, dietary GI and GL were not associated with ischemic CVD or mortality, but dietary GL was associated with a greater risk of hemorrhagic stroke.

Lui, 2000 (positive quality) and **Halton, 2006** (positive quality), both reported relationships between glycemic load and risk of CHD from the Nurses' Health Study. Lui, 2000, prospectively evaluated the relationship between the amount and type of carbohydrates consumed and the risk of CHD. The baseline population was 75,521 women aged 38 to 63 years in 1984. Dietary intake was assessed with an FFQ at baseline and repeated in 1986 and 1990. The primary endpoint considered was CHD, including fatal CHD and non-fatal MI. Non-fatal MI was confirmed by medical records; deaths were identified from the National Death Index and confirmed by medical records, autopsy reports or death certificates. During 10 years of follow-up, 761 cases of CHD were identified. Glycemic load was directly associated with risk of CHD after adjustment for age, smoking status, total energy intake and other coronary disease risk factors; RR of extreme quintiles of glycemic load was 1.98 (95% CI: 1.41, 2.77; P<0.0001). The increased risk of CHD with high glycemic load was most evident among women with BMI>23kg/m^2. Little relation was observed among women with BMI<23kg/m^2. Carbohydrate classified by glycemic index, as opposed to its traditional classification as either simple or complex, was a better predictor of CHD risk. Neither simple sugar nor starch was significantly related to CHD risk when they were included simultaneously in the same multivariate model. In contrast, glycemic index was significantly associated with the risk of CHD in a multivariate model with the same covariates (multivariate adjusted RR comparing extreme quintiles = 1.31; 95% CI: 1.02, 1.68; P=0.008). In a follow-up study, Halton, 2006 prospectively examined the association between low-carbohydrate diet score and the risk of CHD in women. In additional analyses, they examined the relationship between glycemic index or load and CHD. Participants were 82,802 women, aged 30 to 55 years at baseline, who were followed from 1980 to 2000. Dietary intake was assessed with an FFQ at six time points over the study period. The endpoints were non-fatal MI or fatal coronary events. Coronary heart disease was self-reported on questionnaires with confirmation from medical records. Deaths were identified from state records and the National Death Index, next of kin, or the US Postal Service. During 20 years of follow-up, 1,994 cases of CHD were identified. A high glycemic load was strongly associated with an increased risk of CHD (RR comparing extreme deciles = 1.90; 95% CI: 1.15, 3.15; P=0.003). Overall dietary glycemic index had a direct association with risk of CHD (RR comparing extreme deciles = 1.19; 95% CI: 0.91, 1.55; P=0.04).

Oh, 2005 (positive quality), cohort study in the US, prospectively examined associations between dietary carbohydrate, glycemic index (GI), glycemic load (GL) and risk of stroke in 78,779 women who were age 30 to 55 years, free of CVD and diabetes and participants of the Nurses' Health Study. Dietary information was collected for usual diet with a semi-quantitative FFQ. Among the women followed, 1,020 incident strokes were documented (515 ischemic, 279 hemorrhagic). After adjusting for non-dietary risk factors and cerealfiber (CF), carbohydrate intake was found to associate with elevated risk of hemorrhagic stroke when the extreme quintiles were compared (RR=2.05; 95% CI: 1.10, 3.83; P=0.02), but not with ischemic stroke. Carbohydrate intake and dietary GL were positively associated with total stroke among those women whose BMI was higher than 25 kg/m^2 (RR=1.61; 95% CI: 1.15, 2.27; P=0.01), but associations for type of stroke were not statistically significant. Intake of CF was inversely associated with total stroke risk, RR=0.66 (95% CI: 0.52, 0.83; P=0.001) and with hemorrhagic stroke risk, RR=0.51 (95% CI: 0.33, 0.78; P=0.01). Dietary GI was not related to risks of total stroke or type of stroke within BMI categories.

van Dam, 2000 (positive quality), a cohort study in the Netherlands (Zutphen Elderly Study), prospectively examined the association between glycemic index and CHD risk in elderly men. Participants were 646 men, aged 64 to 84 years at baseline, who were followed between 1985 and 1995. Dietary intake was assessed with the cross-check dietary history method. Non-fatal MI information was obtained by physician-administered (in 1985 and 1990) or self-administered (in 1993 and 1995) standardized medical questionnaire. Death information was obtained from the participant's general practitioner and registries. During 4,527 person-years of follow-up, 94 cases of CHD were documented. The multivariate adjusted risk ratio for CHD was 1.11 (95% CI: 0.66, 1.87; P=0.70) for the extreme tertiles of glycemic index after correction for age, BMI, physical activity, cigarette smoking and dietary factors. The multivariate adjusted risk ratio was 1.06 (95% CI: 0.52, 2.14; P=0.88; not adjusted for carbohydrate intake) for the extreme tertiles of glycemic load. The authors concluded that glycemic index or load was not associated with incidence of CHD in elderly men without a history of diabetes or CHD.

Case-control Study:

Tavani, 2003 (neutral-quality), case-control study in Italy, examined the relation between glycemic index and glycemic load and the risk of non-fatal acute MI. Cases were 433 non-diabetic adults with a first episode of non-fatal acute MI, and controls were 448 adults admitted to the hospital for acute conditions unrelated to known or potential risk factors for acute MI. Dietary intake was assessed with a validated FFQ. The odds ratio (OR) in the highest compared to lowest tertile was 1.38 for glycemic index and 1.08 for glycemic load. Neither of these estimates was significant. A significant association was found for glycemic index in patients 60 years and older (OR for highest vs. lowest tertile = 1.81; 95% CI: 1.07, 3.07; P=0.03). A significant association was found for glycemic index in those with a BMI of $25 kg/m^2$ and higher (OR for highest vs. lowest tertile = 2.02; 95% CI: 1.21, 3.34; P=0.006). No other significant associations were observed for BMI, age or gender.

View table in new window

Author, Year, Study Design, Class, Rating	**Population/Subjects**	**Methodology**	**Significant Outcomes**
Beulens JW, de Bruijne LM et al, 2007 Study Design: Prospective Cohort Study Class: B Rating:	N=15,714 women. Age: 49 to 70 years. EPIC Cohort. Location: Netherlands.	Association of glycemic index and glycemic load with incident CVD examined for more than nine years of follow-up. Dietary glycemic index and glycemic load calculated from intake data from FFQs.	141,633 person-years: CHD = 556 cases; CVA = 243 cases. After adjustment for CVD risk and dietary variables, hazard ratios (HR) for CVA: • GL=1.47 (95% CI: 1.04, 2.09; P=0.03) • GI=1.33 (95% CI: 1.07, 1.67; P=0.02). Women with BMI $>25 kg/m^2$: GL=1.78 (95% CI: 1.11, 2.85; P=0.04) vs. normal weight women. Association of GI with CVD not modified by BMI. GI associated with CHD, not CVA (P=0.01).
Halton et al 2006 Study Design: Prospective Cohort Study Class: B	N=82,802 women. Nurses' Health Study. Age: 30 to 55 years at baseline.	Followed from 1980 to 2000. Diet assessed with FFQ at six time points over study period. Endpoints: Non-fatal MI or	During 20 years of follow-up, 1,994 cases of CHD were identified. A high glycemic load was strongly

Rating:	Location: United States.	fatal coronary events; CHD self-reported on questionnaires with confirmation from medical records; deaths identified from state records and the National Death Index, next of kin or US Postal Service.	associated with an ↑ risk of CHD (RR comparing extreme deciles = 1.90; 95% CI: 1.15, 3.15; P=0.003). Overall dietary glycemic index had a direct association with risk of CHD (RR comparing extreme deciles = 1.19; 95% CI: 0.91, 1.55; P=0.04).
Kaushik S, Wang JJ et al, 2009 Study Design: Prospective Cohort Study Class: B Rating:	N=2,712 older participants. Age: 49 years or older. Blue Mountains Eye Study. Location: Australia.	Participants followed for 13 years; inpatients, cause-of-death and death registries for MI, ischemic and hemorrhagic stroke. Mean GI calculated from an Australian database. Retinal arteriolar and venular diameters measured from photographs. Mortality data derived from an Australian National Death Index.	After adjusting for multiple stroke risk factors, ↑ GI (HR=1.91; 95% CI: 1.01, 3.47) and ↓ CF (HR=2.13; 95% CI: 1.19, 3.80) predicted greater risk of stroke death, while there was no relationship between total fruit or vegetable fiber and risk of stroke-related death. Participants consuming food in the highest GI tertiles and lowest CF tertiles had a five-fold ↑ risk of stroke death (HR=5.06, 95% CI: 1.67, 15.22). High-GI and low-CF diets predict greater stroke mortality and wider retinal venular caliber.

Levitan EB, Mittleman MA et al, 2007 Study Design: Prospective Cohort Study Class: B Rating:	N=36,246 men. Age: 45 to 79 years. Location: Sweden.	Baseline assessment: Dietary glycemic index and glycemic load with FFQs. Six-year followed up through inpatient, cause-of-death and death registries: MI, ischemic stroke, hemorrhagic stroke, cardiovascular mortality, all-cause mortality. Cox models with age as time scale to estimate RR adjusted for smoking, BMI, physical activity, demographic characteristics and nutritional factors.	After eight years, dietary glycemic index and glycemic load not linked with: • MI (N=1,324) • Ischemic stroke (N=692) • CV mortality (N=785) • All-cause mortality (N=2,959). Dietary glycemic index linked with hemorrhagic stroke (N=165; HR=1.44; 95% CI: 0.91 to 2.27; P=0.047).
Liu et al 2000 Study Design: Prospective Cohort Study Class: B Rating:	N=75,521 women. Nurses' Health Study. Age: 38 to 63 years at baseline. Location: United States.	Followed from 1984 to 1994. Diet assessed with FFQ at baseline and repeated in 1986 and 1990. Endpoints: Non-fatal MI or fatal CHD; non-fatal MI confirmed by medical records; deaths identified from the National Death Index and confirmed by medical records, autopsy reports or death certificates.	During 10 years of follow-up, 761 cases of CHD were identified. Glycemic load was directly associated with risk of CHD after adjustment for age, smoking status, total energy intake and other coronary disease risk factors. RR of extreme quintiles of glycemic load was 1.98 (95% CI: 1.41, 2.77; P<0.0001). ↑ risk of CHD with high glycemic load was most evident among women with

			BMI >23kg/m^2. Little relation was observed among women with BMI <23 kg/m^2. CHO classified by glycemic index, as opposed to its classification as either simple or complex, was a better predictor of CHD risk. Neither simple sugar nor starch was significantly related to CHD risk when they were included simultaneously in the same multivariate model. In contrast, glycemic index was significantly associated with the risk of CHD in a multivariate model with the same covariates (multivariate adjusted RR comparing extreme quintiles = 1.31; 95% CI: 1.02, 1.68; P for trend = 0.008).
Oh K, Hu FB et al, 2005 Study Design: Prospective cohort study Class: B	N=78,779 women. Nurses' Health Study. Location: United States.	1,980 semi-quantitative FFQ with 61 food items. Followed for 18 years. Stroke endpoint ascertained by medical records (blinded).	Dietary glycemic load, positive association with total stroke in women with BMI >25kg/m^2 (HR=1.61, 95% CI: 1.15, 2.27; P=0.01), but not type of stroke.

Rating:		Non-fatal medically reported strokes – probable (25%). Death ascertained by family reports, postal service and National Death Index. Fatal non-medically reported strokes – probable (32%).	Dietary glycemic index not related to risks of total stroke or type of stroke within BMI categories.
Tavani et al 2003 Study Design: Case-Control Study Class: C Rating:	N=433 cases. N=448 controls. Age: 25 to 79 years. Location: Italy.	Cases: Non-diabetic adults with a first episode of non-fatal acute MI. Controls: Adults admitted to hospital for acute conditions unrelated to known or potential risk factors for acute MI. Dietary intake assessed with validated FFQ.	OR in highest compared to lowest tertile was 1.38 (95% CI: 0.95, 2.00; P=0.10) for glycemic index and 1.08 (95% CI: 0.73, 1.60; P=0.69) for glycemic load (adjusted for sex, age, education, BMI, physical activity, tobacco, alcohol, cholesterol, HTN, hyperlipidemia and family history of IHD). A significant association was found for glycemic index in patients ≥60 years (OR for highest vs. lowest tertile = 1.81; 95% CI: 1.07, 3.07; P=0.03). A significant association was found for glycemic index in those with a BMI of ≥25kg/m^2 (OR for highest vs. lowest tertile = 2.02; 95% CI:

			1.21, 3.34; P=0.006). No other significant associations were observed for BMI, age or gender.
van Dam et al 2000 Study Design: Prospective Cohort Study/Cross-sectional Analysis Class: B Rating:	N=646 men. Zutphen Elderly Study. Age: 64 to 84 years at baseline. Location: Netherlands.	Followed between 1985 and 1995. Dietary intake assessed with the cross-check dietary history method. Non-fatal MI information obtained by physician-administered (in 1985 and 1990) or self-administered (in 1993 and 1995) standardized medical questionnaire. Death information obtained from the participant's general practitioner and registries.	During 4,527 person-years of follow-up, 94 cases of CHD were documented. The multivariate adjusted risk ratio for CHD was 1.11 (95% CI: 0.66, 1.87; P=0.70) for the extreme tertiles of glycemic index after correction for age, BMI, physical activity, cigarette smoking and dietary factors. The multivariate adjusted risk ratio was 1.06 (95% CI: 0.52, 2.14; P=0.88; not adjusted for CHO intake) for the extreme tertiles of glycemic load.

Research Design and Implementation Rating Summary
For a summary of the Research Design and Implementation Rating results, click here.

Worksheets
Beulens JW, de Bruijne LM, Stolk RP, Peeters PH, Bots ML, Grobbee DE, van der Schouw YT. High dietary glycemic load and glycemic index increase risk of cardiovascular disease among middle-aged women: A population-based follow-up study. *J Am Coll Cardiol.* 2007 Jul 3; 50 (1): 14-21. Epub 2007 Jun 18.

Halton TL, Willett WC, Liu S, Manson JE, Albert CM, Rexrode K, Hu FB. Low-carbohydrate-diet score and the risk of coronary heart disease in women. *N Engl J Med.* 2006 Nov 9;355(19):1991-2002.

Kaushik S, Wang JJ, Wong TY, Flood V, Barclay A, Brand-Miller J, Mitchell P. Glycemic index, retinal vascular caliber and stroke mortality. *Stroke.* 2009 Jan; 40 (1): 206-212. Epub 2008 Oct 23.

Levitan EB, Mittleman MA, Håkansson N, Wolk A. Dietary glycemic index, dietary glycemic load and cardiovascular disease in middle-aged and older Swedish men. *Am J Clin Nutr.* 2007 Jun; 85 (6): 1,521-1,526.

Liu S, Willett WC, Stampfer MJ, Hu FB, Franz M, Sampson L, Hennekens CH, Manson JE. A prospective study of dietary glycemic load, carbohydrate intake, and risk of coronary heart disease in US women. *Am J Clin Nutr.* 2000 Jun;71(6):1455-61.

Oh K, Hu FB, Cho E, Rexrode KM, Stampfer MJ, Manson JE, Liu S, Willett WC. Carbohydrate intake, glycemic index, glycemic load and dietary fiber in relation to risk of stroke in women. *Am J Epidemiol.* 2005 Jan 15; 161 (2): 161-169.

Tavani A, Bosetti C, Negri E, Augustin LS, Jenkins DJ, La Vecchia C. Carbohydrates, dietary glycaemic load and glycaemic index, and risk of acute myocardial infarction. *Heart.* 2003; 89(7):722-6.

van Dam RM, Visscher AW, Feskens EJ, Verhoef P, Kromhout D. Dietary glycemic index in relation to metabolic risk factors and incidence of coronary heart disease: the Zutphen Elderly Study. *Eur J Clin Nutr.* 2000 Sep;54(9):726-31.